Changes in Corneal Biomechanical Properties after Laser-Assisted *in situ* Keratomileusis and Photorefractive Keratectomy in Myopia

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ABSTRACT

Objective: To compare changes in corneal biomechanical properties after laser-assisted *in situ* keratomileusis (LASIK) and photorefractive keratectomy (PRK) in low and moderate myopia by Ocular Response Analyzer.

Study Design: Quasi-experimental study.

Place and Duration of the Study: Armed Forces Institute of Ophthalmology (AFIO), Rawalpindi, Pakistan, between September 2020 and April 2022.

Methodology: Myopic correction was done in forty-six eyes of twenty-three patients by PRK, and forty-seven eyes of twenty-four patients by LASIK. Corneal hysteresis (CH) and corneal resistance factor (CRF) were measured using Ocular Response Analyzer (ORA), pre-operatively, and then 1, 3, and 6 months, postoperatively. The relationship between the amount of myopia treated and biomechanical properties was also studied.

Results: CRF and CH were decreased significantly after LASIK and PRK. A significantly larger decrease in CRF was observed after LASIK as compared to PRK at 6 months (Mann-Whitney U test: CRF, $p = 0.02$); however, decrease in CH was not statistically significant between LASIK and PRK at 6 months period (Mann-Whitney U test: CH, $p = 0.388$). A significant correlation was observed between the changes in biomechanical properties and extent of myopic correction after LASIK and PRK.

Conclusion: Biomechanical strength of the cornea was significantly reduced by PRK and LASIK, which was also dependent on the spherical equivalent (SEQ) of myopic correction. A significantly larger change in CRF was observed after LASIK as compared to post PRK.

Key Words: *Myopia, Laser in situ keratomileusis, Photorefractive keratectomy, Cornea, Biomechanics.*

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INTRODUCTION

The rapidly evolving refractive surgery using excimer laser has been stated to be the modern, effective, and safe surgical technique for the rectification of myopia.[1] Even though, people opt more for laser *in situ* keratomileusis (LASIK) than photorefractive keratectomy (PRK), the iatrogenic corneal ectasia that developed after LASIK far exceeds PRK.[2] Moreover, LASIK is a more invasive procedure involving not only stromal ablation but also flap creation of variable thickness; hence, it is likely to weaken corneal strength more as compared to PRK. Studies have proved that the role of anterior corneal stroma in maintaining the corneal biomechanical strength is more than the posterior corneal stroma.[3]

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It is an established fact that the flap made in LASIK has no role in stabilising cornea biomechanically, even after it is repositioned on the stromal bed.[4] All of these findings point to the fact that the corneal biomechanical properties undergoing these two procedures differ postoperatively.

Lately, the Ocular Response Analyzer (ORA) has revolutionised the assessment of corneal biomechanical properties.[5,6] It measures the corneal biomechanical properties using a bi-directional applanation process. The parameters measured by this novel technique like corneal hysteresis (CH) and corneal resistance factor (CRF), are shown to be considerably weakened post LASIK and PRK.[7] CH is the corneal ability to absorb and dissipate energy, hence measuring its viscous damping capacity.[8] It is the corneal response to the deformation caused by an air puff which then is measured by an infrared beam in a waveform, and is greatly influenced by its central corneal thickness (CCT). It has been reported that CCT may relate differently with CH under anomalous corneal conditions. It can be seen that, corneas with similar thickness may have altered biomechanical properties, and vice versa. Thin corneas show lower CH values. Lower CH value is also linked to progressive optic neuropathy and visual field loss, and is an independent risk factor for glaucoma.[9]

The CRF measures corneal resistance to applanate. It is dependent upon central corneal thickness (CCT) and intraocular pressure (IOP) taken by Goldmann Applanation Tonometry (GAT). It has been suggested that the CRF could be primarily associated with the corneal elasticity.[10]

To the best of authors' knowledge, no such study has been conducted on these patients earlier. The objective of the current study was to compare the effects of PRK and LASIK relative to myopic correction on postoperative biomechanical properties of cornea using ORA.

METHODOLOGY

This quasi-experimental study was conducted at the Armed Forces Institute of Ophthalmology, Rawalpindi from September 2020 to April 2022. A formal approval was given by the Institutional Ethical Committee. Written and informed consents were taken from all the patients who participated in the study. Patients with age of more than 18 years with stable refractive error between -2D and -8D for the last one year were included in this study. Patients were excluded from the study if their age was less than 18 years with unstable refractive error, cataract, pregnant or lactating mothers, history of previous ocular pathologies or prior surgeries, corneal pathologies, amblyopia, any posterior segment disease or systemic disease. The purposive sampling technique was used to include one or both eyes of the patient. Those wearing contact lenses were advised a minimum of two weeks discontinuation and a regular use of lubricant before the preliminary evaluation.

Preoperative evaluation included thorough history, examination; that included uncorrected distance visual acuity (UCVA), corrected distance visual acuity (CDVA), cycloplegic refraction, old glasses prescription, detailed anterior and posterior segments examination on slit lamp, intraocular pressure measurement using GAT, tear film break-up time (TBUT) to rule out dry eyes. Corneal topography and pupillometry (Wavelight Topolyzer Vario), corneal tomography (Wavelight Oculyzer II), and aberrometry (Wavelight Analyzer II), all by Wavelight GmbH, Erlangen, Germany were some of the investigations carried out in pre-op assessment of the patients. Corneal biomechanical parameters, i.e. CH and CRF, were recorded using ORA. Patients who fulfilled the eligibility criteria were provided with the complete information about both the procedures, i.e. LASIK and PRK, in form of written materials and videos. All possible benefits, complications, as well as risk of regression, need of presbyopic glasses, and possibility of re-enhancement were discussed by the refractive surgeon and counsellor.

LASIK and PRK were performed by the same experienced surgeon. In both surgical procedures the eyes were topically anaesthetised with 0.5% proparacaine hydrochloride followed by meticulous draping and periocular disinfection with povidone-iodine. Lid speculum was applied and the conjunctival sac was thoroughly irrigated by normal saline. In LASIK, the corneal flap was created using FS 200, 200 kHz Femtosecond laser, (Wavelight GmbH, Erlangen Germany), whereas in PRK, the corneal epithelium was removed manually using PRK spatula. Stromal ablation in both procedures was done by EX 500, 1050 Hz Excimer laser, (Wavelight GmbH, Erlangen Germany). Triangular sponge soaked in 0.02% Mitomycin C was applied on stromal bed in all patients undergoing PRK for 30-40 seconds after stromal ablation. It was then irrigated with balanced salt solution (BSS), and soft bandage contact lens was applied in the end. In all patients undergoing LASIK, the flap size was set at 9mm with a thickness of 100 microns, side cut angle 70 degrees, Optical zone (OZ) 6.5 mm and an ablation zone 9mm. Wave front optimized ablation profile was used for all cases. After the completion of surgery, patients were examined for the status of flap and corneal microstriae at the slit lamp after one hour and prescribed antibiotic plus steroid eye drops (tobramycin and dexamethasone 0.3%/0.1% w/v eye drops) six hourly for two days and then, eight hourly for two weeks, and topical lubricant (combination of polyethylene glycol 400 4mg/ml and propylene glycol 3mg/ml eyedrops) after every two hours. Patients were called for a follow-up the next day. In patients who had undergone LASIK, antibiotic and steroid eye drops were discontinued after 2 weeks while in PRK patients, it was replaced by fluoromethalone eye drops, eight hourly for the next two months. BCL was removed on 6^{th} postoperative day in PRK patients. Lubricants were continued in both procedures for a period of six months.

The main outcome measures were assessed, preoperatively, and then at 1, 3, and 6 months, postoperatively, and it included CH, CRF, manifest refraction spherical equivalent (MRSE), and CCT.

The minimum required sample size of 90 (45 in each group) was calculated by using WHO sample size calculator software, considering effect size of 0.6* (mean postoperative corneal hysteresis difference between the two techniques), pooled standard deviation 1.2*, 95% level of confidence, 80% study power, and a two-tailed hypothesis.[11]

IBM SPSS (version 25.0) was used to perform the statistical analysis. Means and standard deviations (SD) were reported for the continuous variables. The categorical variables were reported as frequency and percentages. For statistical analysis, repeated measures ANOVA with Bonferroni correction, Independent sample t-test, Pearson's correlation, Mann-Whitney U test, and Chi-square test of independence were used to understand the relation between different variables. The significance level was set at $p<0.05$. The normality of the data was assessed using Shapiro-Wilk test.

RESULTS

Myopic correction was done in forty-six eyes of twenty three patients by PRK, and forty-seven eyes of twenty four patients by LASIK. The study population were well-matched in age, CCT, CH, and CRF. Preoperative patients' demographics are shown in Table I.

Table I: Preoperative patients demographics (n=93).

	PRK (n=46)	LASIK (n=47)	p-value
Age in years(a)	23.6 ± 4.2	24.6 ± 6.3	0.385
Gender n (%)(b)			0.014
Male	31 (67.4)	20 (42.6)	
Female	15 (32.6)	27 (57.4)	
Central corneal thickness (CCT)(a)	545.3 ± 23.7	546.8 ± 29.7	0.785
Manifest refraction spherical equivalent (MRSE)(a)	-2.8 ± 1.1	-4.11 ± 1.4	<0.001
Corneal hysteresis (CH)(a)	10.3 ± 1.1	10.4 ± 1.2	0.569
Corneal resistance factor (CRF)(a)	10.3 ± 1.2	10.1 ± 1.6	0.961

(b) Independent sample t-test, (b) Chi-square test of independence.

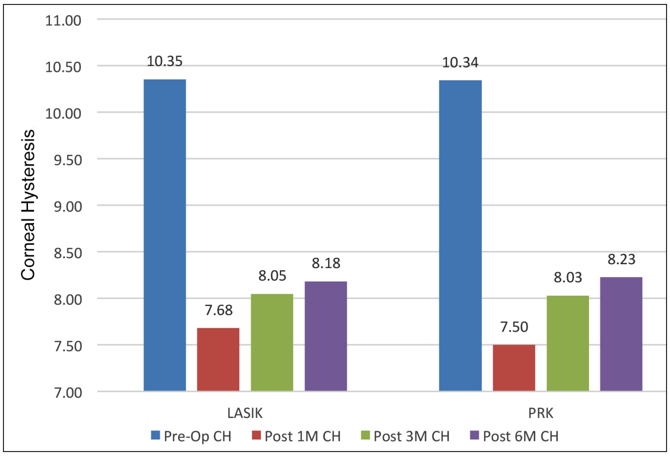

Figure 1a: Changes in CH between preoperative and 1, 3 and 6 months post-operative, in LASIK and PRK.

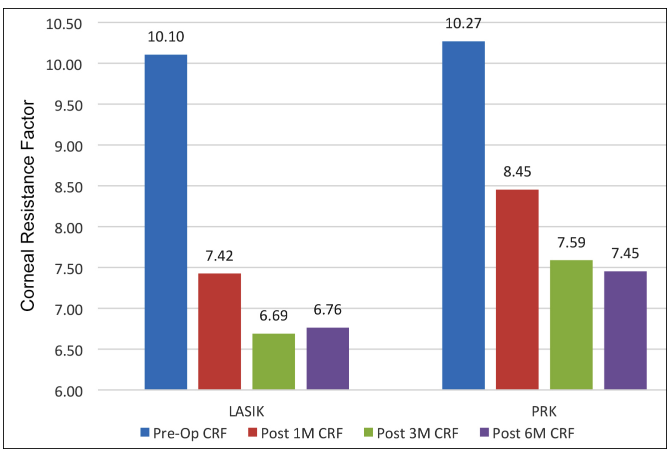

Figure 1b: Changes in CRF between preoperative and 1, 3 and 6 months postoperative, in LASIK and PRK.

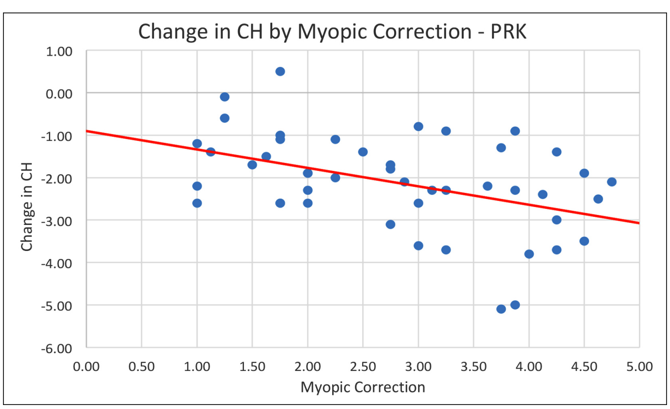

Figure 2a: Change in CH by myopic correction, PRK.

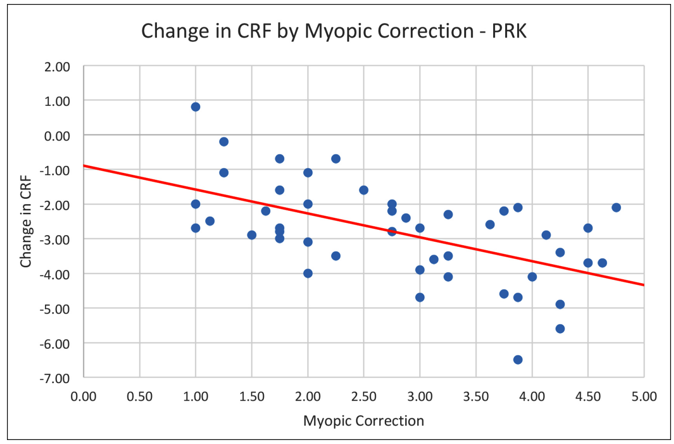

Figure 2b: Change in CRF by myopic correction, PRK.

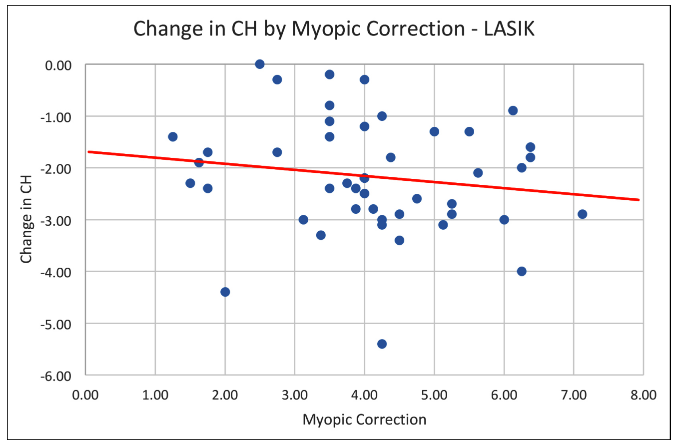

Figure 3a: Change in CH by myopic correction, LASIK.

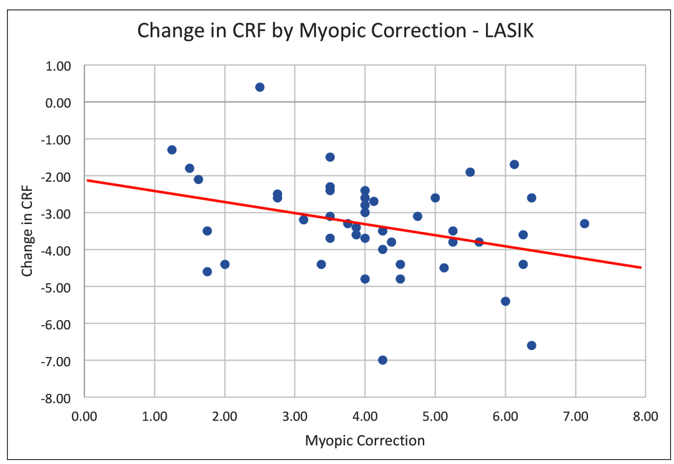

Figure 3b: Change in CRF by myopic correction, LASIK.

CCT decreased significantly from preoperative to 3 months postoperative in both LASIK (546.8 ± 29.7 to 469.1 ± 36.1, p<0.01) and PRK (545.3 ± 23.7 to 487.0 ± 33.9, p<0.01).

Using ANOVA with repeated measures with a Greenhouse--Geisser correction, there was a statistically significant difference in mean scores for CH [F (2.85, 131.4) = 100.38, p<0.001] and CRF [F (1.82, 83.5] = 99.3, p<0.001] at the three follow-up periods after LASIK. Using Bonferroni post-hoc test, it was determined that CH value significantly decreased from preoperative to 1-month postoperative follow-up (10.35 ± 1.2 to 7.68 ± 1.3, p<0.01) mmHg, and then increased from 1 month to 6 months postoperative (7.68 ± 1.3 to 8.18 ± 1.1, p<0.01, Figure 1a). A significant decrease was found in mean CRF values between preoperative to 1-month postoperative (10.10 ± 1.6 to 7.42 ± 1.9, p<0.01) and 1 to 3 month follow-up periods (7.42 ± 1.9 to 6.69 ± 1.2, p<0.01, Figure 1b).

For PRK, the three follow-up periods showed significant difference in mean scores for CH [F (2.4, 106.4) = 112.3, p<0.001] and CRF [(*F*(2.5, 112.8) = 80.4, p<0.001)]. The CH significantly decreased from pre-operative to 1-month postoperative (10.34 ± 1.1 to 7.50 ± 1.3, p<0.01) mmHg, and gradually increased from 1 month to 6 months period which was statistically significant (7.50 ± 1.3 to 8.23 ± 0.9, p<0.01, Figure 1a). The CRF significantly decreased from preoperative to 1-month postoperative (10.27 ± 1.2 to 8.45 ± 1.4, p<0.01), from 1 month to 3 month postoperative (8.45 ± 1.4 to 7.59 ± 1.2, p<0.01, Figure 1b).

A significantly larger decrease in CRF was observed after LASIK as compared to post PRK (Mann-Whitney U test: CRF, p=0.02). There was no significant decrease in CH between LASIK and PRK (Mann-Whitney U test: CH, p=0.388). In the six months follow-up period, iatrogenic keratectasia was not observed in any patient.

A significant correlation was found between the extent of myopic correction and changes in biomechanical properties of the cornea (CH, Pearson correlation coefficient r = –0.425, p=0.003; CRF, r = –0.370, p<0.01) post PRK (Figure 2a and 2b). A notable correlation was also found between the extent of myopic correction and changes in corneal biomechanical properties (CH, r = –0.349, p=0.014; CRF, r = –0.487, p<0.001) post LASIK (Figure 3a and 3b).

DISCUSSION

The changes in biomechanical properties have been a point of focus for refractive surgeries, due to the long-term implications as instability of cornea and ectasia.[12] This study showed that CH was decreased significantly in both LASIK and PKR at one month postoperative, however, there was no statistically significant change in overall decrease in CH between LASIK and PRK. It was further found that CRF decreased more in individuals treated with LASIK than PRK at six months. Similar results were reported by Hwang *et al.*[13] In their study they, highlighted that CH and CRF decrease after both LASIK and PRK, however, the decrease is lower for PRK. They further supported the addition of mitomycin during the procedure as an aid in increasing the CH and CRF after three months of the procedure which partially supported the findings of this study about increase in CH between one and six months postoperative, both in LASIK and PRK. It was also supported by Mohammadi *et al.* where individuals with MMC showed better corneal biomechanical properties as compared to those without MMC.[14] Kamiya *et al.* reported that CH and CRF decreased more post-LASIK as compared to post-PRK (p=0.004).[11]

This study showed that a negative correlation existed between the extent of myopic correction and the amount of CH and CRF decrease. A similar finding was reported by Kamiya *et al,*[11] where they evaluated a negative linear correlation of myopic correction with CH (r = -0.61) and CRF (r = -0.41) in PRK, and CH (r = -0.37) and CRF (r = -0.45) in LASIK. Hence, they concluded that, even though, both procedures had similar effects on decreasing the CH and CRF, the degree of change was greater in LASIK than in PRK. It further suggested that PRK is more efficient for preserving biomechanical properties. Other studies evaluating biomechanical properties after LASIK and PRK also reported that the biomechanical changes decrease more significantly after LASIK than PRK.[14,15] Shen *et al.* also highlighted the negative correlation between the degree of myopia corrected and the change in the corneal biomechanical strength (LASIK r = -0.34).[16]

Similarly, Yildirim *et al.* supported the results of CRF and CH being equally affected among refractive surgeries, with a negative correlation among the extent of correction done with the reduction in the CRF and CH.[17] They suggested that the possible cause of reduction in CRF and CH after any procedure involving the anterior thirds of the cornea is due to the disturbance of collagen fibrils which are in greater amount in the anterior portion of the cornea. The disruption leads to a breakage of linkages and hence, affect, the elasticity of the cornea more. This was also supported by Vanathi *et al.* who suggested a similar negative correlation of CH (r = -0.33) and CRF (r = -0.34) with the percent tissue altered during LASIK.[18] Gatinel *et al.* revealed a greater tissue alteration in LASIK than PRK, which supports better biomechanical properties after PRK than LASIK.[19] However, Raevdal *et al.* published that no significant difference existed among CRF and CH after flap and no-flap surgeries.[20]

CONCLUSION

This study concluded that the CRF and CH decrease significantly after refractive surgeries such as LASIK and PRK. Changes in corneal biomechanics in terms of CRF were significantly larger post-LASIK as compared to post-PRK, and no significant decrease in CH was observed between LASIK and PRK. Also, there is a negative correlation between the degree of myopia corrected and the decrease in CRF and CH. However, considering wound healing response, corneal biomechanical properties should be followed long-term to see the on-going changes.

ETHICAL APPROVAL:
This study was conducted after the approval of Institutional Review Board and Ethical Committee of the Armed Forces Institute of Ophthalmology.

PATIENTS' CONSENT:
All patients gave informed consents to participate in the study.

COMPETING INTEREST:
All authors declared no competing interest.

AUTHORS' CONTRIBUTION:
SH: Conception and design of the work and data analysis.
MI: Interpretation of data and final approval of the manuscript.
YA: Drafting of the work.

HY: Data acquisition.

All authors have approved the final version of the manuscript to be published.

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